UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,444	07/11/2005	Gregor Reid	15339	7350

23389 7590 10/04/2007

SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
10/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,444	REID ET AL.	
	Examiner	Art Unit	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-15 and 17-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9-15, 17-20* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Applicant's amendment filed on 07-26-2007 has been entered. Status of claims. Claims1-7, 9-15, 17-20 are currently pending. Claims 1, 13 and 15 have been amended and claims 8 and 16 have been canceled by Applicant's amendment filed on 07-26-2007. This application contains claims 6 and 12 drawn to an invention nonelected with traverse in the reply filed on 12-22-2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
3. The examiner acknowledges Applicants' reference to Exhibits A-D at pages 8, 15 and 16 of Remarks. Applicants' submission of figures 3, 4, 8, 3.7 (Table 4 and 5) in the Remarks is not labeled as exhibits. Therefore, the examiner has considered figures 3, 4, 8, 3.7 (Table 4 and 5) lacking the label.

Response to Applicant's Remarks

In relation to the species election in the restriction filed on 09-19-2006, Applicants argue on page 5 of Remarks, that both the urogenital and intestinal microbiota "comprise *L. iners*, and indeed the intestine is the source of these organisms for the urogenital tract". Moreover, Applicants cite at page 6 of Remarks, four references in support the presence of *L. iners* in both the instestine and vagina. Further, Applicants state "the consistent wide-ranging

finding of *L. iners* demonstrates clearly its fundamental presence in healthy people of all ages. Applicants respectfully request the Examiner to reconsider the restriction and examine all the strains together". Such is not persuasive.

As disclosed in the previous office action, each of the claimed species, the urogenital and intestinal microbiota, comprise different microorganisms with different structure and functionality, with domination of different strains being influenced by many factors. Though both populations of microbiota comprise *L. iners*, each population comprises different and distinct bacteria resulting in different structures and physiological properties. For example, enzymes produced by micro flora of the small intestine specifically digest food substances (e.g., maltase, lactase, fats) while they are being absorbed through the epithelium. In contrast, bacterial vaginosis in the urogenital tract results when the normal, predominantly *Lactobacillus* vaginal flora shifts to one dominated by *Gardnerella vaginalis*, *Mycoplasma hominis*, and a variety of anaerobic organisms (Ferris et al., J Clin Microbiol. 2007: 1016–1018, Abstract). Thus, the combined features of a specific species, distinct structurally and functionally, would not necessarily overlap with one another when a prior art search is conducted and would impose a serious burden in the examiner

The examiner notices that all the references discloses by applicant on page 6 of Remarks, specifically teach the presence of *L. iners* in the urogenital flora and not in the gastrointestinal flora.

The requirement is still deemed proper and made Final. It is noted that when a final requirement for restriction is made by the examiner, applicant may file a petition under 37 CFR 1.144 for review of the restriction requirement. The propriety of a requirement to

restrict, if traversed, is reviewable by petition under 37 CFR 1.144 . In re Hengehold, 440 F.2d 1395, 169 USPQ 473 (CCPA 1971).

Therefore, claims 1-7, 9-15, 17-20 are being examined to which the following grounds of rejection are applicable.

4. Withdrawn rejections in response to Applicant arguments or amendments.

Claim Rejections - 35 USC § 112- Second Paragraph

In view of applicant amendment of claim 17 to recite "inulin" rejection of claim 17 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been withdrawn.

Claim Rejections - 35 USC § 112- First paragraph- Scope of Enablement

In view of applicants amendment of claim 1 to recite " wherein said *L. iners* is administered orally or vaginally" rejecion of claims 1-7 and 13 under 35 U.S.C. 112, first paragraph, has been withdrawn.

Rejection, Obviousness Type Double Patenting-Second reference

In view of applicants' arguments in relation to the unobvioussness of the strain of Lactobacillus, L. iners Y16329, over the specific strains of Lactobacillus disclosed in U.S. Patent No. 6,479,051 , rejection of claims 1-14, and 18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of

Falsen (International Journal of Systematic Bacteriology, 1999, 217-221) and Nugent et al., (J Clin Microbiol. 1991 29:297-301), has been withdrawn.

In view of applicants' arguments in relation to the unobvioussness of the strain of Lactobacillus, L. iners Y16329, over the specific strains of Lactobacillus disclosed in U.S. Patent No. 6,479,051, rejection of claims 1-14, and 18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen (International Journal of Systematic Bacteriology, 1999, 217-221) and Nugent et al., (J Clin Microbiol. 1991 29:297-301) and further in view of Gibson et al., (Gastroenterology, 1995, 975-82), has been withdrawn.

In view of applicants' arguments in relation to the unobvioussness of the strain of Lactobacillus, L. iners Y16329, over the specific strains of Lactobacillus disclosed in U.S. Patent No. 6,479,051, rejection of claims 1-15 over claims 1, 2, 5-10 of U.S. Patent No. 6,180,100, in view of Falsen (International Journal of Systematic Bacteriology, 1999, 217-221) and Nugent et al., (J Clin Microbiol. 1991 29:297-301), has been withdrawn.

5. ***Rejections maintained in response to Applicant arguments or amendments.***

Claim Rejections - 35 USC § 112- First paragraph- Scope of Enablement

In view of Applicants amendment of claim 1, the scope of enablement has been modified.

Claims 14-15, 17-19 remain rejected and new claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

A method of inhibiting urogenital pathogens colonization of the urogenital tract in women comprising administering a therapeutically effective amount of at least one *Lactobacillus iners* and a pharmaceutically acceptable carrier, wherein said Lactobacillus *iners* is administered orally or vaginally.

The specification does not reasonably provide enablement for a method of maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of at least one *L. iners* by **any route of administration**. Moreover, the specification does not reasonably provide enablement for a method of treatment of **any infection** in a subject as broadly embraced by claim 19. Further, the specification does not provide enabling disclosure for a method of establishing a healthy bacterial flora in a female **throughout life** as encompassed by claim 1.

Response to Applicants' arguments as they relate to rejection of claims 13-15, 17-19 and claim 20 under 35 U.S.C. 112, first paragraph.

It is the Applicants position that the Specification makes clear to those of skill in the art that *L. iners* can be administered in a therapeutically effective dose, and the specfication discloses that administration itself can be in tablets, capsules, food and others. Moreover, Applicants contends that though no prior art discloses that *L. iners* have been shown to provide benefits in respiratory and urinary tracts as other Lactobacilli, evidence exists in support of the effectivenesss of administering *L. iners* for treatment of diseases other than vaginal infections such as to boost CD4 count in HIV/AID patients, reducing the risk of Chlamydia and herpes

infections, reducing the risk of gonococcal or chlamydial genital infection, and even treatment or prevention of cancers (see page 10 of Applicants remarks). As such Applicants argue that one of skill in the art can utilize *L.* iners in a method for treateing **any infection** without undue experimentation. Such is not persuasive

The specification does not provide sufficient guidance for a method for treating any infection in a subject as broadly claimed for the reasons of record and the following reasons.

In relation to the first publication by Anukan et al., (2007, J. Clin. Gastroenterology, in press) Applicants have not provided a copy of the publication; therefore the examiner has not considered the reference.

The Cherpes et al., (Clin Infect Dis. 2003) reference merely discloses a cohort study of sexually active women to identify variables associated with the acquisition of herpes simplex virus type 2 wherein bacterial vaginosis (BV) were associated with HSV-2 seroconversion and the diagnosis of BV remained associated with an increased risk of acquiring HSV-2 infection (Abstract). Hence there is not supporting evidence for the treatment of any disease with L. *iners.*

The Anukam et al., (Sex Transm Dis. 2006) reference teaches that the predominant vaginal Lactobacillus species in African women do not differ substantially to those of white decent (Abstract). Hence there is not supporting evidence for the treatment of any disease with *L. iners.*

Therefore, none of the disclosed references provides enabling disclosure for treatment or reduction of risk of bacterial vaginosis with *L. iners*, let alone treatment or prevention of a genus of unidentified infectious diseases in a human subject as claimed including diseases transmitted by bacteria, viruses, fungi and protozoa. Addtionally, the specification clearly teaches that 19

non-symptomatic women were studied to investigate the effect and persistence of vaginally inserted capsules administered for three days containing viable *lactobacilli*: *L. fermentum* RC-14 and L. *rhamnosus* GR-1 (p. 19). Therefore, it is unclear how a healthy bacterial flora is going to be maintained and extended throughout the life of a woman once therapeutic administration of *L. inners* by orally or vaginally is interrupted. There is no disclosure of any examples or specific guidance for the identification of methods for establishing a healthy bacterial flora in females throughout life as broadly claimed but only during the course of treatment. Hence it would require undue experimentation to determine alternative regimen of administration meeting the claim requirements to establish a healthy bacterial flora in females throughout life.

Further, in relation to claim 19, Applicants argue on pages 10 and 11 of Remarks, that the claim does not exclude co-administration of *L. iners* with anti-viral, or antibiotics or other medications for treatment of any infectious disorder as Applicants have recently shown that probiotic lactobacilli augment the efficacy of antibiotics in treating infections (Anukam et al., 2006, Microbes and Infection). Moreover, Applicants contend that claim 19 is not directed to curing diseases but treating diseases, which is sufficiently supported by the disclosure of the present application. As such, Applicants argue that one skilled in the art can utilize the appropriate lactobacilli in a method for treating any infection, without undue experimentation. Such is not persuasive.

In relation to claim 19, the scope of the invention as embraced by claim 19 is not commensurate with the disclosure of the as filed evidence because the instant claim encompasses treatment of widely divergent infectious diseases in terms of their pathologic mechanisms. For

example, it seems likely that a cellular treatment of a cell population that is an effective treatment with antibiotics for infectious diseases caused by a bacteria such as diphtheria, would unlikely be effective at treating sexually transmitted diseases such as cervical cancer, or AIDS caused by Herpes or HIV viruses. The disclosure of the Anukan et al., publication (2006, Microbes and Infection), further supports the lack of predictability of treating any disease as the disclosed treatment is limited to enhancement of the efficacy of orally administered metronidazole, which is an antibiotic well known in the art for the treatment of bacterial vaginosis, in conjuction with oral administration of *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14, which are Lactobacilli also well known in the art for their ability to colonize the vagina. Thus, given the unpredictability of the art and the lack of working example in the instant specification, one of ordinary skill in the art is no enable to make and use a therapeutic effective amount of *Lactobacillus iners* for the treatment of any disease by any route of administration in a human subject, as broadly claimed.

In so far as the term "curing" vs. "treating" by administering a therapeutically effective amount, the specification does not provide any closed definition as to what is meant by a "therapeutically effective amount" to result in "treatment of an infection" but defines "therapeutically effective amount" as the amount of probiotic organism, e.g., Lactobacillus iners, high enough to significantly positively modify the condition to be treated but low enough to avoid serious side effects (p. 8, paragraph 3; p. 14, paragraph 3). As such, and in view of the customary and ordinary meaning of the term "cure" in the art as "restoration to health after a disease, or to bring about recovery from, or remedy " (Webster's Seventh New Collegiate

Dictionary, G. C. Merriam Co.), the term cure is embraced by a method for "treatment of an infection".

Claim Rejections - 35 USC § 102

Claim 15 remain rejected under 35 U.S.C. 102(e) as being anticipated by Falsen et al., Journal of Systematic Bacteriology, 1999, 217-221.

Response to Applicants' arguments as they relate to rejection of claim 15 under 35 USC § 102.

On page 12 of Applicants remarks, Applicants argue, "that nowhere does the Falsen et al. reference disclose a pharmaceutical composition comprising *L. iners*, a prebiotic and a pharmaceutically acceptable carrier". Such is not persuasive

As stated in the previous office action, the as-filed specification defines a "pharmaceutically-acceptable carrier" as any one or more compatible solid or liquid able of being commingled without substantially decreasing the pharmaceutical efficacy of the composition (p. 11). Thus the pharmaceutical composition can be broadly interpreted as any media that comprises *L. iners* without affecting the efficacy of the composition (e.g., water). Further, the as-filed specification defines a prebiotic as "a nonmetabolized, nonabsorbed substrate that is useful for the host which selectively enhances the growth and/or the metabolic activity of a bacterium or a group of bacteria. A prebiotic also includes a nutrient utilized by lactobacilli or bifidobacteria to stimulate and/or enhance growth of lactobacilli or bifidobacteria relative to pathogenic bacteria" page 5. Therefore, a prebiotic broadly encompasses any growth

media that enhances the growth of the bacteria (e.g., serum added to the media). Therefore, the Falsen et al., publication by teaching a new isolated species of Lactobacillus: *L. inners* that growths in an agar culture supplemented with 5% horse blood at 37C in air plus CO_2, which is further prepared in SDS (Sodium Dodecyl Sulfate) for protein quantification, anticipates the instant invention.

New Grounds of Rejection

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 3 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language.

Claim 3 is vague and indefinite in that the metes and bounds of the phrase "Lactobacillus iners is Y16329" are unclear. It is unclear why Lactobacillus inner is identified with the number Y16329. It would be remedial to amend the claim language to indicate the American Type Culture Collection (ATCC).

Claim 20 recite the limitation "displacing vaginal pathogens". The specification discloses at page 7, last paragraph that "the Lactobacillus iners of the present invention will **inhibit growth and/or adhesion** of enteric pathogens to gastrointestinal surfaces", at page 13, paragraphs 2 and 3, that "The introduction or administration of lactobacilli probiotics to the intestine and passage onto the urogenital tract ... ...stimulates host responses are stimulated

which **inhibit pathogens** and/or create a microenvironment less conducive to pathogen spread", and "combination of adhesion of Lactobacillus iners and the production by Lactobacillus iners of one or more inhibitory substances is responsible for **excluding pathogens** and/or reducing their numbers at the site of a gastrointestinal or genito-urinary infection". Therefore it is unclear whether "displacing vaginal pathogens" refers to inhibiting binding other vaginal pathogen or competing with pathogens already bound to the vaginal mucosa to unbound them. The metes and bounds of the claims are not clear.

Claim Rejections - 35 USC § 112- First paragraph- New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 20 recite the limitation "displacing vaginal pathogens". Applicants cite at page 8 of remarks support for new claim 20 in the Specification at page 10, last paragraph. However, Applicants' referred paragraph relates to formulations for compositions. The specification discloses at page 7, last paragraph that "he Lactobacillus iners of the present invention will **inhibit growth and/or adhesion** of enteric pathogens to gastrointestinal surfaces", at page 13,

paragraphs 2 and 3, that "The introduction or administration of lactobacilli probiotics to the intestine and passage onto the urogenital tract ... ...stimulates host responses are stimulated which **inhibit pathogens** and/or create a microenvironment less conducive to pathogen spread", and "combination of adhesion of Lactobacillus iners and the production by Lactobacillus iners of one or more inhibitory substances is responsible for **excluding pathogens** and/or reducing their numbers at the site of a gastrointestinal or genito-urinary infection". No other teachings are disclosed of "**displacing vaginal pathogens**". Thus is not clear that the Applicant was in possession of a genus of undefined "**displaced vaginal pathogens**" at the time the application was filed.

Conclusion

Applicant response filed on 07-26-2007 has been considered by the Examiner but is moot in view of the new grounds of the rejection, which is necessitated by the claims amendment. THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding his application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Maria Leavitt, PhD
Patent Examiner P/1633
Remsen 2B55
Phone: 571-272-1085

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633